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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,078	10/07/2003	Jeannette Whitcomb	011068-067-999	6233
20583	7590	02/22/2008	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			LI, BAO Q	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/681,078	Applicant(s) WHITCOMB, JEANNETTE	
	Examiner BAO LI	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 93-307 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 93-207 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08) | 5) ☐ Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) ☐ Other: _____ |

DETAILED ACTION

Petition of Revival

The petition for revive the unintentionally abandoned Application has been granted and mailed out on Jan 31, 2008.

RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Oct/31/2007 has been entered. The RCE follows:

Response to the Amendment after Final

The amendment and response filed on Oct. 31, 2007 after final has been acknowledged and entered. Claim 93 has been amended. Claims 1-93 and 98-103 were canceled. Claims 93-97 and 104-107 are pending and considered before the examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 93-97 and 105 are still rejected under 35 U.S.C. 102(b) as being anticipated by Petropoulos et al. (WO 99/67427A1) for the same ground as stated in the previous Office Action.

3. Applicants traverse the rejection and argue that Petropoulos et al. do not teach each and every element of the claimed method. In particular, they do not teach that the presence of the particular mutations recited by claims 93-97 correlate with decrease in NNRTI susceptibility. As such, Petropoulos et al. cannot teach a method that comprises, inter alia, determining that an HIV has increased replication stimulated by an anti-viral drug.

4. Applicants' argument has been fully considered; however, it is not found persuasive. Because the particular mutation at codon 245 in combination with at least other mutation located

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at one codon 98, 101, 103, 138, 181, 190 or 225 associated with NNRTI induced RT resistance is also described by Petropoulos et al. as the target for determining whether HIV has reduced NNRTI susceptibility.

5. Regarding the limitation of determining increased replication stimulated by an antiviral drug, it is worthy to note that the actually practice for determining the increases replication associated by an anti-RT drug described by the specification comprises a). collecting a biological sample from an HIV infected patient, (b) evaluating whether the biological sample comprises nucleic acid encoding HIV RT gene mutation and c).analyzing if the presence of a mutation by RT-PCT and sequencing. Petropoulos et al. teach a same method that involves collecting the HIV infected samples from a patients inherently after monitoring the viral replication condition and detecting if there is any mutation associated by the anti-RT agent including NNRTI resistant strain, wherein the possible mutation codons particularly includes 245 in combination with other NNRTI induced mutation such as Y181C/I that is cited in the rejected claims. Moreover, it is well know that once the HIV is mutated to an anti-RT agent including a NNRTI, a rapid virus replication reoccurs instead of decrease in the presence of RT inhibitor. Because the re-busted HIV replication increase is caused by the HIV mutation induced by the NNRTI or other RT inhibitor treatment, the virus replication is considered to be induced or stimulated by an anti-RT agent treatment. Therefore, the claimed method is still inherently anticipated by the cited reference. The rejection is maintained.

6. Upon reconsidering the pending claims, a new ground rejection has been made on the record set forth below:

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 93-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining a biological sample of a mutant HIV-1 that contains a triple mutations at the codons V245E/T in combination of K103N and

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I135T, wherein the mutant has the claimed phenotype of a reduced NNRTI susceptibility and increased replication stimulated by an antiviral drug of NNRTI, does not reasonably provide enablement for having a method of determining a biological sample of any HIV mutant, and a HIV mutant has mutated on codons V245E/T in combination with any kind of combination of codon 98 or 101, 103 or 135, 138, 181, 190 or 225, and the phenotype change of increased viral replication can be induced by any or all kinds of antiviral drugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

9. The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or Unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

10. The nature of the invention is drawn to a method for determining whether an HIV-1 infected patient has reduced NNRT treatment susceptibility. The method comprises detecting if the HIV-1 strain has a triple mutation of V245E/T in combination with K103N and I135T. However, the claims are broadly directed a method can be practiced with detecting any combination of amino acid substitutions or mutation of 245 with at least one of mutation at codon 98, 101, 103, 135, 138, 181, 190 and 225. This constitutes a rather large genus of variants which are not supported by the disclosure, wherein any or the genotype as it is claimed would have same phenotype of reducing the susceptibility of NNRTI treatment and increase viral replication induced by any antiviral drug. For instance, would the skilled artisan reasonably expect GI90W and KI01H to display increased/decreased susceptibility to NNRTIs.

11. State of art teaches that non-nucleoside reverse transcriptase inhibitors (NNRTIs) have more than thirty structurally different classes of compounds capable of specifically inhibiting

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HIV-1 replication by interacting at the specific binding sites (pocket) of HIV-1 RT gene. But these sites are distinct from the nucleoside reverse transcriptase inhibitors (NRTIs) as evidenced by Erik De Clercq (Farmaco 1999, Vol. 54, pp. 26-45, see entire document, especially Fig. 9). As such, only NNRTI agents can induce the increased HIV replication that is associated with the particular mutated codons as claims drafted. Moreover, Applicants' own disclosure also teaches that the increase viral replication is limited to the V245E/T in combination with two additional mutations at the codons K103N and I135T triple mutations. The mutation V245E/T in combination with either K103N or I135T alone does not exhibit the phenotype of drug-dependent stimulation of viral replication in the presence of NNRTIs including nevirapine, efavirenz, or delavirdine (see pages 104-105 of the specification). Therefore, it is unpredictable that all claimed mutants can have the claimed phenotype and also any or all antiviral drugs can induce the same genotype mutation as claims drafted. Moreover, the prior art teaches that limited numbers of substitutions are associated with increased/decreased NNRTI drug resistance (Bacheler et al., 2001; Ceccherini-Silberstein *et al.*, 2007).

12. The specification only teaches that HIV-1 mutant with a triple mutation of V245E/T, K103N and I135T is able to produce the claimed phenotype change. The specification teaches that the V245E/T with either K103N or I135T would not exhibit the increased virus replication. The disclosure of the specification also fails to provide sufficient guidance pertaining to the presence of the claimed mutations in the human immunodeficiency virus type 2 (HIV-2) RT. Although HIV-1 and -2 are both lentiviruses, they only display ~35-38% genetic relatedness at the nucleotide sequence level. Accordingly, considering the genetic unrelatedness between these two viruses, it seems improbable that the same mutations in HIV-1 RT would be present in the HIV-2 RT.

13. Thus, the skilled artisan would readily question the ability of other mutations at the disclosed location to produce a mutant RT with the desired phenotype.

14. Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention in a manner commensurate in scope with the claims.

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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/

Primary Examiner, Art Unit 1648